

WHAT IS CLAIMED IS:

1                    1.    A nucleic acid molecule comprising an aptamer and a polynucleotide  
2    that encodes a transcriptional regulatory polypeptide, wherein binding of a ligand to the  
3    aptamer inhibits translation of the transcriptional regulatory polypeptide.

1                    2.    The nucleic acid of claim 1, wherein the ligand is a cell-permeable  
2    small organic molecule.

1                    3.    The nucleic acid of claim 2, wherein the ligand is Hoechst dye 33258.

1                    4.    The nucleic acid of claim 1, wherein the ligand is a metal ion.

1                    5.    The nucleic acid of claim 1, wherein the ligand is an antibiotic.

1                    6.    The nucleic acid of claim 1, wherein the ligand is a steroid.

1                    7.    The nucleic acid of claim 1, wherein the transcriptional regulatory  
2    polypeptide is a repressor.

1                    8.    The nucleic acid of claim 1, wherein the transcriptional regulatory  
2    polypeptide is a transcriptional activator.

1                    9.    The nucleic acid of claim 1, wherein the transcriptional regulatory  
2    polypeptide is a coactivator.

1                    10.    The nucleic acid of claim 1, wherein the transcriptional regulatory  
2    polypeptide comprises a DNA-binding domain.

1                    11.    The nucleic acid of claim 10, wherein the DNA-binding domain is  
2    that of a protein selected from the group consisting of E2F-1, GAL4, a STAT protein, a  
3    steroid/thyroid receptor protein, a Cys2-His2 zinc finger DNA binding motif, and a  
4    tetracycline repressor.

1                    12.    The nucleic acid of claim 1, wherein the transcriptional regulatory  
2    polypeptide comprises a transcriptional repressor domain.

1                    13.    The nucleic acid of claim 12, wherein the transcriptional repressor  
2    domain is that of a protein selected from the group consisting of Rb protein, v-erbA, retinoic

3 acid receptor alpha, thyroid hormone receptor alpha, yeast Ssn6/Tup1 protein complex,  
4 SIR1, NeP1, TSF3, SFI, WT1, Oct-2.1, E4BP4, KRAB and ZF5.

1 14. The nucleic acid of claim 12, wherein the transcriptional repressor  
2 domain is that of p53.

1 15. The nucleic acid of claim 1, wherein the transcriptional regulatory  
2 polypeptide comprises a transcriptional activation domain.

1 16. The nucleic acid of claim 1, wherein the nucleic acid is an mRNA  
2 molecule.

1 17. The nucleic acid of claim 16, wherein the mRNA is bound to a ligand.

1 18. An expression cassette that comprises a promoter operably linked to a  
2 polynucleotide from which is transcribed the nucleic acid of claim 1.

1 19. An expression vector that comprises the expression cassette of  
2 claim 18.

1 20. The expression vector of claim 19, wherein the expression vector is a  
2 viral vector.

1 21. The expression vector of claim 20, wherein the viral vector is selected  
2 from the group consisting of an adenoviral vector, a retroviral vector, and an adeno-  
3 associated viral vector.

1 22. The expression vector of claim 19, wherein the expression vector is a  
2 nonviral vector.

1 23. The expression vector of claim 19, wherein the expression vector  
2 further comprises a second polynucleotide, wherein transcription of the second  
3 polynucleotide is regulated by the transcriptional regulatory polypeptide.

1 24. The expression vector of claim 23, wherein the second polynucleotide  
2 encodes a therapeutic polypeptide.

1                   25.     The expression vector of claim 23, wherein the second polynucleotide  
2 is operably linked to a binding site for the transcriptional regulatory polypeptide.

1                   26.     A cell that comprises the nucleic acid molecule of claim 1.

1                   27.     The cell of claim 26, wherein the cell further comprises a second  
2 polynucleotide, wherein transcription of the second polynucleotide is regulated by the  
3 transcriptional regulatory polypeptide.

1                   28.     The cell of claim 27, wherein the second polynucleotide is included in  
2 the nucleic acid.

1                   29.     The cell of claim 27, wherein transcription of the second  
2 polynucleotide yields an antisense nucleic acid.

1                   30.     The cell of claim 27, wherein the second polynucleotide encodes a  
2 polypeptide.

1                   31.     The cell of claim 30, wherein the polypeptide is a therapeutic  
2 polypeptide.

1                   32.     The cell of claim 31, wherein the therapeutic polypeptide is selected  
2 from the group consisting of a toxin, a cytokine, a kinase, a phosphatase, a transcriptional  
3 regulatory protein, an antibody, and a tumor suppressor.

1                   33.     The cell of claim 32, wherein the polypeptide is a tumor suppressor.

1                   34.     The cell of claim 33, wherein the tumor suppressor is p53.

1                   35.     The cell of claim 26, wherein the cell further comprises a ligand that  
2 binds to the aptamer.

1                   36.     A method of regulating expression of a gene, the method comprising:  
2                   contacting with an aptamer-binding ligand an RNA that comprises an aptamer  
3 and a polynucleotide that encodes a transcriptional regulatory polypeptide that regulates  
4 expression of the gene;

5 wherein the ligand binds to the aptamer, thus inhibiting translation of the  
6 transcriptional regulatory polypeptide resulting in a change in the expression level of the  
7 gene.

1 37. The method of claim 36, wherein the change in the expression level of  
2 the gene is proportional to the amount of aptamer-binding ligand administered.

1 38. The method of claim 36, wherein the transcriptional regulatory  
2 polypeptide is a repressor, whereby binding of the ligand to the aptamer inhibits translation  
3 of the repressor thus causing an increase in the expression level of the gene.

1 39. The method of claim 36, wherein the transcriptional regulatory  
2 polypeptide is a transcriptional activator, whereby binding of the ligand to the aptamer  
3 inhibits translation of the transcriptional activator thus causing a decrease in the expression  
4 level of the gene.

1 40. The method of claim 36, wherein the gene comprises a binding site for  
2 the transcriptional regulatory polypeptide.

1 41. The method of claim 36, wherein the gene is included in a  
2 chromosome.

1 42. The method of claim 36, wherein the gene is extrachromosomal.

1 43. The method of claim 36, wherein the mRNA is contained in a cell.

1 44. The method of claim 43, wherein the cell is part of a multicellular  
2 organism.

1 45. The method of claim 44, wherein the contacting is accomplished by  
2 administering the ligand to the organism.

1 46. The method of claim 36, wherein the RNA is transcribed from an  
2 expression cassette that comprises a promoter operably linked to a polynucleotide from  
3 which is transcribed the RNA.

1 47. The method of claim 46, wherein the promoter is a constitutive  
2 promoter.

1                   48.    A method of retarding undesirable cell proliferation, the method  
2 comprising administering to undesirably proliferating cells:  
3                   a nucleic acid construct that comprises a promoter operably linked to a  
4 polynucleotide, wherein the polynucleotide is transcribed to yield an mRNA that comprises  
5 an aptamer and a polynucleotide sequence that encodes a transcriptional regulatory  
6 polypeptide that regulates expression of a gene involved in regulation of cell proliferation;  
7                   an aptamer-binding ligand that binds to the aptamer;  
8                   wherein the binding of the ligand to the aptamer inhibits translation of the  
9 transcriptional regulatory polypeptide, thus causing a change in the expression level of the  
10 gene, which change in expression level ameliorates the undesirable cell proliferation.

1                   49.    The method of claim 48, wherein the gene involved in regulation of  
2 cell proliferation is a tumor suppressor gene and the transcriptional regulatory polypeptide is  
3 a repressor, whereby binding of the ligand to the aptamer results in an increase in the tumor  
4 suppressor gene expression level.

1                   50.    The method of claim 48, wherein the gene involved in regulation of  
2 cell proliferation is a transgene.

1                   51.    The method of claim 50, wherein the gene comprises a promoter  
2 operably linked to a polynucleotide that encodes a polypeptide involved in regulation of cell  
3 proliferation.

1                   52.    The method of claim 51, wherein the promoter is a constitutive  
2 promoter.

1                   53.    The method of claim 50, wherein the gene is included on an  
2 expression vector that is administered to the undesirably proliferating cells.

1                   54.    The method of claim 53, wherein the expression vector further  
2 comprises the nucleic acid construct.

1                   55.    The method of claim 48, wherein the nucleic acid construct is  
2 included on an expression vector that is administered to the undesirably proliferating cells.